General

Guideline Title

ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors.

Bibliographic Source(s)

Roberts CC, Kransdorf MJ, Beaman FD, Adler RS, Amini B, Appel M, Bernard SA, Fries IB, Germano IM, Greenspan BS, Holly LT, Kubicky CD, Lo SS, Mosher TJ, Sloan AE, Tuite MJ, Walker EA, Ward RJ, Wessell DE, Weissman BN, Expert Panel on Musculoskeletal Imaging. ACR Appropriateness CriteriaÂ® follow-up of malignant or aggressive musculoskeletal tumors. Reston (VA): American College of Radiology (ACR); 2015. 15 p. [83 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Fitzgerald JJ, Roberts CC, Daffner RH, Weissman BN, Appel M, Bancroft L, Bennett DL, Blebea JS, Bruno MA, Fries IB, Germano IM, Hayes CW, Holly L, Kransdorf MJ, Luchs JS, Morrison WB, Olson JJ, Scharf SC, Stoller DW, Taljanovic MS, Tuite MJ, Ward RJ, Wise JN, Zoga AC, Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 13 p. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Follow-up of Malignant or Aggressive Musculoskeletal Tumors

Variant 1: Lower risk patient (low grade). Evaluation for metastatic disease to the lung from musculoskeletal primary. Baseline examination at time of diagnosis.

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	9	Despite some of the cost analysis studies, the panel believes early diagnosis of lung metastases is critical and that chest CT should be performed. If chest CT is done, chest x-ray is not necessary.	☢☢☢
PET/CT skull base to mid-thigh	1,2,3 Usually not appropriate	4,5,6 May be appropriate	7,8,9 Usually appropriate	☢☢☢☢

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation

Radiologic Procedure	Rating	Comments	RRL*
		problem-solving tool. Outcomes data on FDG-PET/CT are pending. The CT portion of FDG-PET/CT, although unenhanced, can include thin-section images through the whole body, which can enhance diagnosis.	
X-ray chest	3		☢
CT chest with contrast	1		☢☢☢
CT chest without and with contrast	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Lower-risk patient (low grade). Evaluation for metastatic disease to the lung from musculoskeletal primary. Follow-up examination 3–6 months after treatment or surgery.

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	9	Follow up every 3–6 months for 5 years. After 5 years, frequency can decrease to every 6–12 months.	☢☢☢
FDG-PET/CT whole body	4	This procedure can be a useful problem-solving tool if another study is equivocal.	☢☢☢☢
X-ray chest	3		☢
CT chest with contrast	1		☢☢☢
CT chest without and with contrast	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Higher-risk patient (high grade). Evaluation for metastatic disease to the lung from musculoskeletal primary. Baseline examination at time of diagnosis.

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	9	Despite some of the cost analysis studies, the panel believes early diagnosis of lung metastases is critical and that chest CT should be performed. If chest CT is done, chest x-ray is not necessary.	☢☢☢
FDG-PET/CT whole body	7	In individual cases, this procedure can be a good problem-solving tool. FDG-PET/CT appears to be emerging as a primary diagnostic tool for diagnosing metastatic disease in many musculoskeletal tumors.	☢☢☢☢
X-ray chest	2		☢
CT chest with contrast	1		☢☢☢
CT chest without and with contrast	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Higher-risk patient (high grade). Evaluation for metastatic disease to the lung from musculoskeletal primary. Follow-up examination 3–6 months after treatment or surgery.

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	9		☢☢☢
FDG-PET/CT whole body	5	This procedure can be a useful problem-solving tool if another study is equivocal.	☢☢☢☢
X-ray chest	2		☢
CT chest with contrast	1		☢☢☢
CT chest without and with contrast	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Evaluation for osseous metastatic disease from musculoskeletal primary. Asymptomatic. Baseline and follow-up examination.

Radiologic Procedure	Rating	Comments	RRL*
FDG-PET/CT whole body	2	Although additional imaging should be provided only if the patient is symptomatic, it should be noted that in many cases, baseline whole-body FDG-PET/CT or MRI would already have been done, which provides high sensitivity for some bone tumors.	☢☢☢☢
Tc-99m bone scan whole body	2		☢☢☢
MRI whole body without contrast	2		O
MRI whole body without and with contrast	2		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: Evaluation for osseous metastatic disease from musculoskeletal primary. Symptomatic. Baseline and follow-up examination.

Radiologic Procedure	Rating	Comments	RRL*
FDG-PET/CT whole body	7	In individual cases, this procedure can be a good problem-solving tool. Sclerotic lesions are more difficult to detect with PET but are well demonstrated on the CT portion of the FDG-PET/CT examination.	☢☢☢☢
Tc-99m bone scan whole body	5	Useful screening tool. In cases of abnormal spine uptake, SPECT/CT can be used to better distinguish metastases from degenerative changes.	☢☢☢
MRI whole body without contrast	5	This procedure has demonstrated superior sensitivity and diagnostic accuracy compared to FDG-PET/CT. The value of this modality must be balanced against the time necessary to accomplish the study and the inconsistent availability of the expertise needed to interpret it.	O
MRI whole body without and with contrast	1		O

Radiologic Procedure	Rating	Comments	RRL*
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: Osseous tumor, without significant hardware present. Local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
X-ray area of interest	9	Both MRI and x-ray are indicated.	Varies
MRI area of interest without and with contrast	9	Both MRI and x-ray are indicated. Contrast administration is helpful for further evaluation of equivocal findings.	O
MRI area of interest without contrast	8	Both MRI and x-ray are indicated.	O
FDG-PET/CT whole body	4	This procedure can be a useful problem-solving tool if another study is equivocal.	☢☢☢☢
CT area of interest without contrast	4	On a case-by-case basis, CT can be useful. This procedure is useful for osseous tumors when better definition of bony anatomy is needed.	Varies
CT area of interest without and with contrast	4		Varies
CT area of interest with contrast	3		Varies
US area of interest	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: Osseous tumor, with significant hardware present. Local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
X-ray area of interest	9		Varies
MRI area of interest without contrast	7	Metal suppression techniques can be used.	O
MRI area of interest without and with contrast	7	Metal suppression techniques can be used. Contrast administration is helpful for further evaluation of equivocal findings. Since fat suppression is inhomogeneous with adjacent hardware, pre- and postcontrast subtraction postprocessing is recommended.	O
FDG-PET/CT whole body	5	This procedure can be a useful problem-solving tool if another study is equivocal.	☢☢☢☢
CT area of interest without contrast	5	This procedure can be useful if MRI is not informative. Alter technique to decrease metal artifact.	Varies
CT area of interest with contrast	5		Varies
CT area of interest without and with contrast	2		Varies
US area of interest	2		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 9: Soft-tissue tumors. Local recurrence surveillance. Follow-up examination 3–6 months after treatment or surgery.

Radiologic Procedure	Rating	Comments	RRL*
MRI area of interest without and with contrast	9	Contrast administration is helpful for further evaluation of equivocal findings. Follow-up every 3–6 months for 5 years. After 5 years, frequency can decrease to every 12 months, or the follow-up can be performed earlier if symptomatic.	O
MRI area of interest without contrast	8		O
FDG-PET/CT whole body	6	This procedure can be a useful problem-solving tool if another study is equivocal. Outcomes data on FDG-PET/CT are pending. The CT portion of FDG-PET/CT includes thin-section images through the whole body, which can enhance diagnosis.	☢☢☢☢
CT area of interest with contrast	5		Varies
US area of interest	5		O
X-ray area of interest	2	This procedure can be a problem-solver if needed to interpret findings on MRI.	Varies
CT area of interest without contrast	2	Postoperative scarring can obscure local recurrence.	Varies
CT area of interest without and with contrast	2		Varies
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

This topic specifically excludes 1) metastatic disease from nonmusculoskeletal primaries, 2) head and neck tumors, 3) spine tumors, 4) chest wall tumors, 5) multiple myeloma, and 6) benign or nonaggressive bone or soft-tissue tumors. Evaluation for chemotherapy or radiation therapy effectiveness, preoperatively after induction therapy, is also not included.

It should be noted that there are no controlled studies in the literature that directly address the issue of tumor follow-up, and the recommendations are based on consensus of the American College of Radiology (ACR) Appropriateness Criteria Expert Panel on Musculoskeletal Imaging, are subject to changes if new data come out, and should be used only as a guideline with generous opportunity for modification in individual circumstances.

This topic addresses two issues of follow-up for tumor therapy: the timing of the follow-up examination, and the type of imaging best used.

Ideally, the timing of follow-up for tumor recurrence or metastatic disease would be individualized for each tumor type and each patient. To design a follow-up protocol, one would generally wish to know the following: 1) How good is the imaging test to be used for detecting the presence of tumor? 2) How important is early detection of relapse in relation to salvage effectiveness (utility/risk analysis)? and 3) When is the relapse most likely to occur (hazard rate)? Individual hazard rate is related to tumor type, grade, size, and central location; patient age and gender; tumor stage; type of treatment; and surgical margins. Overall, the goal of an imaging protocol is to concentrate testing when the relapse is most likely to occur. This presumes that testing frequency should gradually decrease over time. There are outstanding reviews of model development for such protocols in lymphoma and other tumors. However, such models do not exist for extremity tumors.

Because models relating to the hazard rate and utility/risk analysis do not exist for individual extremity bone and soft-tissue tumor types, the expert panel will consider the sarcomas as a group and try to evaluate general local recurrence rate and timing as well as metastatic rate and timing. The most helpful general information can be found in previously published practice guidelines. The information most commonly agreed to among these authors is that approximately 80% of patients who recur locally or systemically will do so within 2 to 3 years of their primary treatment. This

suggests that the most aggressive follow-up should occur in the first 2 years, with tapering of imaging after that time. The risk of relapse never drops to zero, so lifetime surveillance is warranted.

Overview

The incidence of metastatic disease from sarcomas varies considerably in the large studies and is dependent on length of follow-up. Metastatic disease only to the lung involves about a third of patients. In one study of extremity soft-tissue sarcomas, there was no significant difference in distant metastases or death from disease in patients who either did or did not have a local recurrence. In at least some of these studies, it appears as though the incidence of local recurrence is less frequent than the occurrence of metastatic disease in high-grade sarcomas, although the adequacy of local therapy is one of the crucial factors determining durable local tumor control. Therefore, local failure may not be the initiating factor in most systemic metastases. This finding suggests that follow-up studies should include systemic surveillance as well as imaging for local recurrence. Although the prognosis for patients with metastatic disease is poor, surveillance is warranted because early detection and treatment of locally recurrent and metastatic disease can prolong survival.

The specific type of imaging for follow-up to check for local recurrence will depend on the site of the original tumor (osseous versus soft tissue) as well as the type of therapy used (including curettage with bone graft versus resection with allograft versus soft-tissue resection, all taking into account the presence or absence of hardware). The following comments relate to each of these situations.

Discussion of Imaging Modalities by Variant

Variants 1, 2, 3, and 4: Metastatic Disease to Lung in Lower-Risk and Higher-Risk Patients

Of the systemic metastases, lung metastasis is by far the most frequent. It is generally accepted that computed tomography (CT) is more accurate in diagnosing lung parenchymal metastatic disease than is chest radiography. However, that increased accuracy may not translate to a positive cost-benefit analysis. One study retrospectively assigned patients to a low- or high-risk theoretical protocol. The incremental cost-effectiveness ratio was $731,000 for routine chest CT imaging to detect each additional case of metastatic disease. Based on this finding, those authors recommend reserving CT selectively for high-risk patients. It has also been suggested that CT be used to follow nodules that are not visible on radiographs and for surgical planning of metastasectomy. Another study favored the use of CT due to increased survival in patients undergoing pulmonary metastatic disease surveillance with CT compared with chest radiography. Given the higher accuracy of CT, as well as the fact that pulmonary metastases from sarcomas are frequently cured by surgical excision or radiofrequency ablation, it is likely that the use of CT for staging and surveillance for lung metastases will continue.

In terms of frequency of follow-up, some experts recommend that high-risk patients have follow-up every 3 to 4 months for the first 2 to 3 years, every 6 months for up to 5 years, and then annually. Patients with low-grade sarcomas should have follow-up every 4 to 6 months for 3 to 5 years and then annually afterward. Recommendations from the National Comprehensive Care Network for soft-tissue sarcomas are based on the stage of the tumor. Stage I sarcomas receive chest imaging every 6 to 12 months for 2 to 3 years. Stage II–IV sarcomas receive chest imaging every 3 to 6 months for 2 to 3 years and then annually thereafter. The optimal frequency and modality of follow-up imaging have not been scientifically established.

Variants 5 and 6: Osseous Metastases from Musculoskeletal Primary

The frequency of distant metastatic disease, other than to lung, ranges from 14% to 20%. It is debatable whether surveillance for osseous metastases or lymphatic metastatic disease is cost efficient. If required, technetium bone scan or positron emission tomography (PET)/CT is most frequently used. Where available, whole-body magnetic resonance imaging (WB-MRI) can detect osseous metastases with good sensitivity and high specificity. Opposed phase gradient echo sequences are useful to improve specificity when equivocal marrow changes are seen on MRI.

The use of fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET)/CT has been shown to be effective in localizing metastases from many bone sarcomas, though it may be nonspecific and produces false negatives in osteosarcoma bone metastases. Although bone scan, FDG-PET/CT, and MRI may detect osseous metastases, these studies are generally not advocated as part of the initial workup or follow-up for osseous metastases in asymptomatic cases.

With regard to screening for osseous metastases, a group of authors showed that coronal whole-body and sagittal spine MRI using T1-weighted and short tau inversion recovery sequences was superior to FDG-PET/CT in sensitivity and diagnostic accuracy. Another group found that fast Dixon WB-MRI had 89% specificity and was more sensitive than bone scan for detecting bone metastasis. A meta-analysis showed WB-MRI to have a pooled sensitivity of 89.9% and specificity of 91.8%. They also found WB-MRI to be cost effective. Thus, in centers that have the capability to do WB-MRI, this is a good alternative to FDG-PET/CT or bone scan and has the added benefit of lacking ionizing radiation exposure.

There is a paucity of recent literature regarding whole-body bone scan and screening for osseous metastases. Much of this likely relates to recent

advances in FDG-PET/CT and WB-MRI and their superior anatomic resolution and specificity. Nonetheless, whole-body bone scan remains a useful screening tool in osseous metastatic disease, with an overall sensitivity comparable to that of FDG-PET/CT. In cases where there is abnormal radiotracer uptake in the spine, single-photon emission computed tomography (SPECT)/CT can be used to better distinguish metastases from degenerative changes, thus increasing specificity.

Metastatic disease from primary extremity liposarcoma deserves special note. A retrospective study of 45 patients with myxoid liposarcoma found that all metastases were extrapulmonary, with the spine and paraspinal soft tissues being most commonly involved. This study also reports a local recurrence at 7.7 years postoperative and new metastatic disease occurring over 10 years postoperative. Thus, a biopsy-proven primary myxoid liposarcoma in the trunk or retroperitoneum should prompt a rigorous search for an occult extremity primary. A subsequent prospective study following 230 patients with myxoid liposarcoma showed that the great majority of patients who developed metastatic disease had a bone metastasis as their first metastatic focus. Of these, the vast majority of the metastases were in the spine. Thus, it seems reasonable that screening MRI of the spine be performed in patients newly diagnosed with or being followed for a myxoid liposarcoma. FDG-PET/CT has a high false-negative rate for detecting myxoid liposarcoma metastases and should be avoided as the primary screening modality.

Alveolar rhabdomyosarcoma also commonly metastasizes outside the lung. This tumor has an unusual pattern of spread, including in-transit, lymph node, bone marrow, pancreas, and bone metastases. Although it has been suggested that metastatic disease surveillance should be different than routine sarcoma, no specific recommendations exist for alveolar rhabdomyosarcoma. Nodal metastases have been reported with extraosseous myxoid chondrosarcoma, but again, no specific recommendations exist for this tumor type.

Variants 7 and 8: Surveillance for Local Osseous Tumor Recurrence with and without Significant Hardware

MRI is the mainstay for evaluation of soft-tissue or bone sarcoma diagnosis and recurrence. MRI provides excellent delineation of the soft tissues and is an even more powerful tool in postoperative imaging due to advances in metal artifact suppression. MRI is useful both for surveillance and directed re-evaluation in cases with clinical concern. There has been a relative paucity of research studies in the literature within the last 10 years regarding the effectiveness of MRI in this clinical situation, but this is likely due to its widespread routine clinical use. MRI has been shown to be efficacious in differentiating between recurrent tumor and post-treatment changes, although some studies were focused on other aspects of tumor research beyond MRI. The majority of the more recent literature focuses on accurate diagnosis of post-treatment changes versus tumor recurrence.

One reference suggests that patients treated with curettage and bone grafting can successfully have recurrences detected with gadolinium-enhanced MRI. In addition to enhanced MRI, both radiographic and CT imaging of treated bone tumors are useful. Imaging findings include enhancement of soft-tissue masses, osteolysis, cortical derangement, development of characteristic matrix, and alteration of the curetted cavity.

In addition to MRI, radiographic evaluation of the area of prior tumor is an important additional adjunct for the interpretation of the MRI examination.

In evaluating whether CT or MRI is more efficacious in follow-up of sarcomas, one should discount articles performed over a decade ago as MRI has dramatically improved over the years since the studies were performed. CT remains useful for imaging of patients who have contraindications to MR scanning and for evaluation of osseous changes, particularly when metal artifact cannot be overcome on MRI. With regard to CT imaging of the abdomen and pelvis for metastatic surveillance after Ewing sarcoma, this practice should not be routinely performed.

Metal artifact associated with allograft treatment of bone sarcomas has historically been a challenge to overcome for surveillance imaging of recurrent tumor and previously necessitated the use of radiographs or radionuclide imaging. However, advancements in metal suppression technique for both CT and MRI have made both of these modalities powerful tools for detection of recurrent tumor and complications. Postoperative imaging recommendations that include references to MR or CT imaging in cases where there is no significant metal artifact can be more broadly applied with implementation of metal artifact suppression techniques.

Extracorporeal irradiation and reimplantation of bone involved with tumor is a relatively uncommon treatment therapy. Surveillance for recurrent tumor in this treatment scenario has been effective using dynamic contrast-enhanced MRI.

There has been a significant amount of literature exploring the use of FDG-PET and FDG-PET/CT in evaluating recurrent soft-tissue and osseous sarcoma. Virtually all clinical studies today are done with FDG-PET/CT, which is reasonably expected and has been proven to be a more powerful tool than FDG-PET alone. Thus, studies regarding the effectiveness of FDG-PET alone are not considered for this discussion.

FDG-PET/CT is a strong rival to MRI for local and distant tumor surveillance due to the anatomic data obtained from thin-slice CT through the entire body and functional tumor metabolism assessment from maximum standardized uptake value (SUV_{max}) measurements. FDG-PET/CT is highly sensitive and specific for detection of bone and soft-tissue sarcoma recurrence. It also has higher diagnostic accuracy than contrast-enhanced CT alone. FDG-PET/CT outperformed conventional imaging with MRI, CT, and bone scan in a series of 13 children with

rhabdomyosarcoma, resulting in a change in lymph node staging, bone involvement, and treatment. Potential limitations of the CT portion of a FDG-PET/CT study include lack of intravenous contrast and lack of breath-hold technique. Bone lesions identified on FDG-PET are not always visible on CT. Although FDG-PET/CT has a high positive predictive value when findings are concordant, the positive predictive value has been shown to markedly decrease when findings are discordant.

One study showed that the SUV_{max} obtained with FDG-PET/CT can predict prognosis in osteosarcoma. A high SUV_{max} before chemotherapy correlated with worse progression-free survival. A high SUV_{max} after chemotherapy correlated with both a worse progression-free survival and poor overall survival. A decrease in SUV_{max} after chemotherapy correlated with >90% tumor necrosis and good overall and progression-free survival. Along these lines, the SUV_{max} can be used to detect recurrence of metastatic lung lesions that have been treated with radiofrequency ablation.

Drawbacks of FDG-PET/CT relative to MRI include higher radiation exposure with subsequent cancer risk and decreased availability of this technology.

Additional outcomes data for FDG-PET/CT are expected as a result of the National Oncologic PET Registry (www.cancerpetregistry.org). Future studies will likely expand on the use of additional radiotracers such as 18 F-fluoride and PET/MRI.

Timing of Surveillance for Local Recurrence

Local recurrence can be as low as 9% to 12% at 5 and 10 years using multimodality therapy as well as limb-sparing surgery and may be routinely as low as 10% in patients with high-grade sarcomas <5 cm at the time of diagnosis. Local recurrence ranged from 4.1% to 23.4% in several large studies. Different studies have related local failure to tumor grade and type of resection. A multivariate analysis found histologic type and absence of wide resection to statistically impact local recurrence. A group of authors found that local recurrence was significantly impacted by having an intermediate/high grade tumor and having multifocally positive surgical margins. They also found that local recurrence predicted an increased chance of metastasis and worsened survival. The impact of a local recurrence on survival varies in the literature. Another group also found that local recurrence and microscopically positive surgical margins correlated with worsened survival. In another study, long-term survival was influenced only by local control of tumor, and local relapse was related to surgical margins, radiation therapy, and histologic type. Another study noted that patients with a positive surgical margin are 3.76 times more likely to have a local recurrence, but having a recurrence did not change survival. Patients undergoing limb amputation for local control of tumor have been found to have a 3 times higher risk of mortality. Failing to resect a core needle biopsy tract was not found to increase local recurrence (8.5%) in a study where all patients received adjuvant therapy, including radiation (97%) and chemotherapy (83%), and that used the literature as a comparison group.

Because of the different findings regarding the importance of local recurrence in survival, it seems reasonable to establish a suggested timing sequence for evaluating local recurrence, with the caveat that for marginal excision and intermediate- to high-grade tumor, more frequent follow-up may be efficacious. One retrospective analysis drawing on a review of 1500 patients from the Memorial Sloan-Kettering Cancer Center and the MD Anderson Cancer Center recommended follow-up of adult soft-tissue sarcomas based on low and high risk of recurrence. Risk stratification was based on size of primary neoplasm (T1: low risk, <5 cm; T2: high risk, >5 cm). For local recurrence in low-risk patients, the recommendation was for "cross-sectional imaging of choice" individualized for patient and location of primary tumor. The implication is that for extremity primaries, the clinical examination may obviate the need for routine cross-sectional imaging follow-up in the low-risk group. Cross-sectional imaging follow-up for less accessible areas (trunk or retroperitoneum) would be required at 3 to 4 month intervals for 2 years, 4 to 6 month intervals for 2 years, and yearly thereafter. Within the low-risk group, one could consider stopping surveillance after 5 to 10 years, although local recurrence has been documented at over 11 years after resection.

Within the high-risk group, the local recurrence rate was noticeably higher, and the analysis recommended cross-sectional imaging every 3 months for 2 years, every 4 months for the next 2 years, every 6 months for the fifth year, and then annually. A study looking at soft-tissue sarcoma patients who were alive and without recurrence or metastasis at 5 years showed that the size and grade of tumor predicted adverse events. Of those living patients, the late relapse rate was 6.3%, which led to 50% mortality. An analysis of high-grade soft-tissue sarcomas found that poor overall survival was associated with tumor size, particularly >8 cm, and the presence of metastasis before tumor resection. Regarding particular tumor histologic types, synovial sarcomas have a propensity to metastasize after 5 years. These data may necessitate a more tailored approach to follow-up of patients with bone or soft-tissue sarcoma, especially those with particular histologic primaries, large tumor size, presence of presurgical metastasis, and positive surgical margins.

Very few follow-up MRI protocols have been advocated. However, a group of researchers suggest an algorithm for following soft-tissue tumors postoperatively. This algorithm starts with T2 imaging. If a mass is present on T2-weighted imaging, it should be followed by T1-weighted sequences with and without contrast. This procedure generally distinguishes hematoma and seroma from tumor or inflammation. If necessary, this procedure can be followed by dynamic enhanced imaging with subtraction postprocessing, which further helps differentiate tumors from

inflammation. In this algorithm, if a region of high signal intensity is seen on T2-weighted imaging but there is no mass present, further evaluation with contrast imaging is not recommended. They state that there will be some exceptions to the above recommendations. Contrast may be particularly helpful when assessing for recurrence in the presence of postoperative hematoma and assessing the acuity of bone metastases. Based on these authors' experience, they advocate delaying the postoperative baseline scan for at least 6 to 8 weeks to allow postoperative changes to subside.

Variant 9: Soft-Tissue Tumors, without Significant Hardware Present. Local Recurrence Surveillance. Follow-up Examination 3 to 6 Months after Treatment or Surgery

As noted above, MRI is the mainstay to evaluate for recurrent soft-tissue tumors. FDG-PET/CT has emerged as a powerful tool for evaluating local recurrence, particularly in the face of suboptimal cross-sectional imaging because of large amounts of metal. FDG-PET/CT and its possible applications are addressed separately above. It has recently been suggested that surveillance imaging for recurrent soft-tissue sarcomas be done only in the setting where the primary tumor site is difficult to evaluate clinically.

Recurrence involving only the soft tissues can also be detected by ultrasound (US). No recent studies specifically advocate the use of US over MRI in follow-up for soft-tissue masses, although US is a cost-effective alternative in many cases. As with studies comparing MRI to CT, studies comparing US to MRI that are over a decade old should be discounted due to technologic advances. US may be particularly useful in the presence of extensive hardware, with a palpable clinical concern for recurrence or for surveillance of easily accessible operative sites. Color Doppler flow imaging can help differentiate recurrent tumor mass from fibrous tissue or other nonvascular tissue in the postoperative tumor site; this was shown to be helpful in the presence of hardware and if there is a baseline postoperative Doppler study.

Summary of Recommendations

- In patients with a musculoskeletal primary malignancy and either a high or low risk for metastatic disease, surveillance for pulmonary metastases should be performed using a CT scan of the chest without contrast. The baseline postoperative examination should occur within 3 to 6 months. Additional chest CT scans should be performed every 3 to 6 months for the first 10 years, although after 5 years a decrease in frequency to every 6 to 12 months can be considered on an individual basis.
- Osseous metastatic disease from a musculoskeletal primary malignancy should be imaged only if symptomatic. Osseous metastatic disease screening utilizing MRI can be considered in patients with myxoid liposarcoma, as these patients have a disproportionately high rate of soft-tissue and bone metastases compared with other musculoskeletal primary neoplasms. Whole-body FDG-PET/CT has a high false-negative rate for myxoid liposarcoma metastases and should not be considered a first-line screening tool for this tumor type.
- Baseline imaging of the tumor area should be performed 3 to 6 months postoperatively. Follow-up imaging should occur every 3 to 6 months for 10 years. After 5 years, a decrease in frequency to every 12 months can be considered on an individual basis. Additional imaging should occur earlier if the patient becomes symptomatic.
- For surveillance of osseous tumor local recurrence, without significant hardware present, both radiographs and an MRI with or without contrast of the area of interest are indicated. If significant hardware is present, radiographs should be obtained, and an MRI may be attempted using metal suppression techniques. Whole-body FDG-PET/CT can be a useful problem-solving tool if study findings are equivocal.
- For evaluation of soft-tissue tumor local recurrence, MRI of the area of interest with or without contrast is recommended. Whole-body FDG-PET/CT is useful as a problem-solving tool if MRI is equivocal.

Abbreviations

- CT, computed tomography
- FDG-PET, 2-fluorine-18 fluoro-2-deoxy-D-glucose-positron-emission tomography
- MRI, magnetic resonance imaging
- Tc-99m, technetium-99 metastable
- US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a		

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

- Malignant or aggressive musculoskeletal tumors
- Metastatic disease

Note: This guideline specifically excludes:

- Metastatic disease from nonmusculoskeletal primaries
- Head and neck tumors
- Spine tumors
- Chest wall tumors
- Multiple myeloma
- Benign or nonaggressive bone or soft-tissue tumors

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Internal Medicine

Nuclear Medicine

Oncology

Radiology

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To address two issues regarding follow-up for tumor therapy: the timing of the follow-up examination and the type of imaging best used

Target Population

Patients with malignant or aggressive musculoskeletal tumors

Note: Patients evaluated for chemotherapy or radiation therapy effectiveness, preoperatively after such induction therapy, are not included.

Interventions and Practices Considered

1. Computed tomography (CT)
    - Chest without contrast
    - Chest with contrast
    - Chest without and with contrast
    - Area of interest without contrast
    - Area of interest with contrast
    - Area of interest without and with contrast
2. 2-fluorine-18 fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography (FDG-PET/CT), whole body
3. X-ray
    - Chest
    - Area of interest
4. Technetium (Tc)-99m bone scan, whole body
5. Magnetic resonance imaging (MRI)
    - Whole body without contrast
    - Whole body without and with contrast
    - Area of interest without and with contrast
    - Area of interest without contrast
6. Ultrasound (US) area of interest
7. Timing, frequency, and duration of follow-up examinations

Major Outcomes Considered

- Utility and diagnostic accuracy of radiologic examinations in detecting metastatic disease
- Frequency and duration of follow-up
- Recurrence rates
- Overall and progression-free survival rates

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 55 citations in the original bibliography, 15 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in December 2013 to identify additional evidence published since the *ACR Appropriateness Criteria® Follow-up of Malignant or Aggressive Musculoskeletal Tumors* topic was finalized. Using the search strategy described in the literature search companion (see the "Availability of Companion Documents" field), 57 articles were found. Seven articles were added to the bibliography. Fifty articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased, or the articles were already cited in the original bibliography.

The author added 61 citations from bibliographies, Web sites, or books that were not found in the new literature search.

Number of Source Documents

Of the 55 citations in the original bibliography, 15 were retained in the final document. The new literature search conducted in December 2013 identified seven articles that were added to the bibliography. The author added 61 citations from bibliographies, Web sites, or books that were not found in the new literature search.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development documents (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND/UCLA Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. An initial survey is conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness (additional assumptions regarding rating appropriateness can be found in the document Rating Round Information). When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the first rating round, a conference call is scheduled to discuss the evidence and, if needed, clarify the variant or procedure description. If there is still disagreement after the second rating round, the recommendation is "may be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

One study retrospectively assigned patients to a low- or high-risk theoretical protocol. The incremental cost-effectiveness ratio was $731,000 for routine chest computed tomography (CT) imaging to detect each additional case of metastatic disease. Based on this finding, those authors recommend reserving CT selectively for high-risk patients. It has also been suggested that CT be used to follow nodules that are not visible on radiographs and for surgical planning of metastasectomy.

A meta-analysis found whole-body magnetic resonance imaging (WB-MRI) to be cost effective.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria (AC).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 83 references cited in the *ACR Appropriateness Criteria® Follow-up of Malignant or Aggressive Musculoskeletal Tumors* document, 63 are categorized as diagnostic references including 7 good quality studies and 16 quality studies that may have design limitations. Additionally, 20 references are categorized as therapeutic references including 14 good quality studies. There are 46 references that may not be useful as primary evidence.

While there are references that report on studies with design limitations, 21 good quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate selection and timing of radiologic imaging procedures for follow-up of patients with malignant or aggressive musculoskeletal tumors

Potential Harms

- Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography (FDG-PET/CT) has a high false-negative rate for detecting myxoid liposarcoma metastases and should be avoided as the primary screening modality.
- The use of FDG-PET/CT has been shown to be effective in localizing metastases from many bone sarcomas, though it may be nonspecific and produces false negatives in osteosarcoma bone metastases.
- A drawback of FDG-PET/CT relative to magnetic resonance imaging (MRI) includes higher radiation exposure with subsequent cancer risk.

Relative Radiation Level

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria (AC) and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR AC through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.
- It should be noted that there are no controlled studies in the literature that directly address the issue of tumor follow-up, and the recommendations in the original guideline are based on consensus of the ACR Appropriateness Criteria Expert Panel on Musculoskeletal Imaging, are subject to changes if new data come out, and should be used only as a guideline with generous opportunity for modification in individual circumstances.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Roberts CC, Kransdorf MJ, Beaman FD, Adler RS, Amini B, Appel M, Bernard SA, Fries IB, Germano IM, Greenspan BS, Holly LT, Kubicky CD, Lo SS, Mosher TJ, Sloan AE, Tuite MJ, Walker EA, Ward RJ, Wessell DE, Weissman BN, Expert Panel on Musculoskeletal Imaging. ACR Appropriateness CriteriaÂ® follow-up of malignant or aggressive musculoskeletal tumors. Reston (VA): American College of Radiology (ACR); 2015. 15 p. [83 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Musculoskeletal Imaging

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Fitzgerald JJ, Roberts CC, Daffner RH, Weissman BN, Appel M, Bancroft L, Bennett DL, Blebea JS, Bruno MA, Fries IB, Germano IM, Hayes CW, Holly L, Kransdorf MJ, Luchs JS, Morrison WB, Olson JJ, Scharf SC, Stoller DW, Taljanovic MS, Tuite MJ, Ward RJ, Wise JN, Zoga AC, Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 13 p. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2015 Sep. 3 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2015. 129 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors. Evidence table. Reston (VA): American College of Radiology; 2015. 35 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors. Literature search. Reston (VA): American College of Radiology; 2015. 1 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on May 6, 2001. The information was verified by the guideline developer as of June 29, 2001. This summary was updated by ECRI on May 22, 2003. The updated information was verified by the guideline developer on June 23, 2003. This summary was updated on August 11, 2006. This summary was updated by ECRI Institute on June 29, 2009. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on July 7, 2011. This summary was updated by ECRI Institute on January 20, 2016.

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